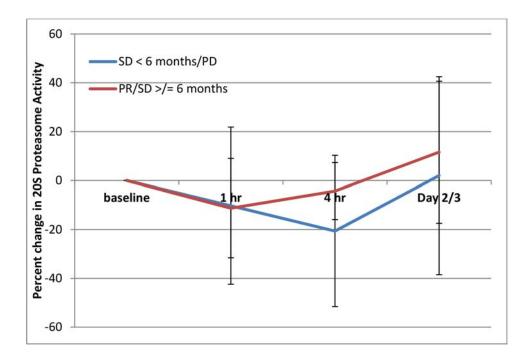
## **SUPPLEMENTARY DATA**

Table S1: HIF- $1\alpha$  expression before and after treatment

Patient	Predose Biopsy				Post-Dose Biopsy					
Diagnosis	Best Response	Months on Study	HIF1	% positive	Intensity	Location	HIF1	% posi- tive	Intensity	Location
Nasopharyngeal	SD (-21%)	6	No tissue in biopsy sample			+	100%	1/2	cytoplasm	
Prostate	SD (-19%)	5	+	100%	3	cytoplasm	+	40%	2	cytoplasm + nucleus
Fallopian Tube	SD (-15%)	8	+	100%	2	cytoplasm	-	n/a	n/a	n/a
Granular Cell Carcinoma	SD (-8%)	5	No tissue in biopsy sample				-	n/a	n/a	n/a
GE junction	SD (5%)	2	Tissue block could not be located			-	n/a	n/a	n/a	
Bladder	Clinical PD	1	+	70%	3	cytoplasm	Biopsy not performed			
Colorectal	Clinical PD	2	+	100%	1/2	cytoplasm	Biopsy not performed			
Paraganglioma	Clinical PD	< 1	-	n/a	n/a	n/a	Biopsy not performed			
Renal Cell	Clinical PD	1	+	100%	3	cytoplasm	-	n/a	n/a	n/a
Prostate	PD (23%)	1	+	40%	1/2	cytoplasm + nucleus	-	n/a	n/a	n/a
Melanoma	PD (38%)	2	+	90%	Variable (1-3)	cytoplasm	Tissue block could not be located			
SCC H&N	Inevaluable (PD)	< 1	+	100%	3+	cytoplasm	Biopsy not performed			
Rectal	Inevaluable	< 1	+	100%	1/2	cytoplasm	Biopsy not performed			
Renal Cell Carcinoma	Inevaluable	1	-	n/a	n/a	n/a	+	90%	2+	cytoplasm

<sup>&</sup>quot;+" = positive, "-" = negative Intensity measured on a scale of 1-3 gray box = no sample





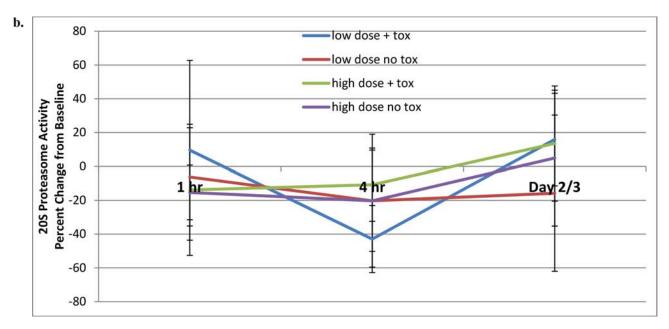


Figure S1: 20S Proteasome Inhibition. (a). Mean change in 20S proteasome activity stratified by response. Percent change in 20S proteasome activity from 31 patients was analyzed. Patients with PR or SD  $\geq$  6 months (n = 3) were analyzed in one group (red line) while patients with SD < 6 months or PD (n = 28) were analyzed in a second group (blue line). (b). Mean change in 20S proteasome activity stratified by high/low dose and +/— toxicity. Percent change in 20S proteasome activity from 31 patients was analyzed. Patients were stratified by dose levels and then further stratified by specific toxicities experienced (Grade 2 or greater thrombocytopenia, diarrhea, nausea, vomiting, and/or neuropathy vs. other). Eight patients received lower dose levels of bortezomib of 0.7-1.0 mg/m² and did not experience specified Grade  $\geq$ 2 toxicities (red line) while three patients received lower dose levels of bortezomib and did experience Grade  $\geq$ 2 toxicities (blue line). Nine patients received higher dose levels of bortezomib and did not experience specified Grade  $\geq$ 2 toxicities (purple line) while 11 patients received higher dose levels of bortezomib and did experience Grade  $\geq$ 2 toxicities (green line).